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TITLE: Management Options for Women at Risk for Inherited Breast Cancer in a Multi-ethnic Health Plan Population: A Randomized Control Trial

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13. Abstract (Maximum 200 Words) (abstract should contain no proprietary or confidential information) This project has addressed possible differences by ethnicity and socioeconomic status in the family history of breast cancer, and in the knowledge and attitudes of women who may be interested in testing for inherited susceptibility to breast cancer. The aims of this study are: a) to survey a population-based, ethnically diverse sample to examine relationships between family history of breast cancer, knowledge of and attitudes toward genetic testing for inherited susceptibility, and sociodemographic factors, such as education and ethnicity; b) to conduct focus groups with Asian, Hispanic, African American, and White women to learn about possible differences in their attitudes concerning genetic testing.  A new aim was planned and developed during the last year. The third aim is to follow-up the survey respondents from Aim 1 to determine the influence of the respondents' family history of breast cancer, ethnicity, and knowledge and attitudes towards breast cancer and genetic testing on their use of genetic counseling and genetic testing, and use of services such as mammography and pap tests in the 4-5 years elapsed since the original survey. This annual report describes our progress in developing and conducting the follow-up study planned as Aim 3.				
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## **Introduction**

Most research on factors involved in genetic testing for inherited susceptibility to breast cancer has focused on the small percentage of women who are at high risk due to a strong family history of breast or ovarian cancer. Of course, the great majority of women have family histories that confer low to moderate risk of inherited susceptibility of BRCA1 or BRCA2, but these women may still be interested in learning about the role that family history and genetic factors play in development of breast cancer and may desire education about the pros and cons of genetic testing.

This study had three aims: a) to survey a large, population-based, ethnically diverse sample of women in order to better understand the relationships among family history of breast and ovarian cancers, knowledge of and attitudes toward genetic testing for inherited susceptibility, and sociodemographic factors such as education and ethnicity; b) to conduct focus groups for samples of Asian, Hispanic, African American, and White women in order to learn more about differences in their values and attitudes concerning genetic testing; and c) to conduct a randomized controlled trial of several educational interventions designed to educate women from diverse backgrounds about the pros and cons of genetic testing. During the last year, we requested and received permission to change our statement of work, substituting a follow-up study of the cohort of women surveyed 4-5 years ago for the third aim of the study, which had been made irrelevant by secular changes.

## **Body**

### **1. Development of Manuscript Reporting Results of Survey of Family History, Screening Behavior and Attitudes Toward Testing in a Multiethnic Sample**

A principal focus of work during the period 9/2000 – 8/2001 was the continuing preparation of a manuscript for publication of results of the survey.

The survey inquired in some detail about the woman's family history of breast and ovarian cancer, her own cancer history, breast screening practices, knowledge about and attitudes toward genetic testing for inherited susceptibility to cancer, demographic factors (including ethnicity and education), as well as several questions concerning the woman's perceived susceptibility to breast cancer in comparison to a) other women her age, b) women with a different family history, and c) women from other ethnic groups.

A probability sampling scheme based on census block characteristics was devised to yield a sample that was 20% each African-American, Asian, and Hispanic, and 40% non-Hispanic white. The survey was mailed to 16,171 eligible women, ages 25 to 70 years. The survey was completed by 9,873 women for a response rate of 65.2%, including 6,967 women who responded to the mailed survey and 2,906 women who completed telephone interviews. The resulting sample was representative of the groups the sample was designed to study. Self-identification was 42.5% non-Hispanic white, 17 and 18%,

respectively, Asian and Hispanic, and 22% African American. The sample was approximately equally distributed over four age groups with 20-28% in each group.

This was the first population-based survey of family history and perception of risk to include significant proportions of all major ethnic groups except for Native Americans. Results showed that only 2% of women had family histories with 2 or more first or second degree relatives with breast cancer. The overwhelming majority of women –about 87% -- reported no family history of breast cancer. Analyses of different ethnic groups indicated that family history varied by ethnicity, with somewhat higher numbers of whites and African Americans reporting family histories that conferred moderate or high risk when compared with the reported family histories of Asian and Hispanic women.

Significant differences were found between ethnic groups in the perception of risk of breast cancer for women from the same ethnic background. High numbers of African American women perceived the risk to African Americans as higher than in other groups, while Asians perceived the risk among Asians as much lower than others, and whites perceived their risk as about the same as all other groups.

Women cannot reliably report on family history or personal history of ovarian cancer, as evidenced by comparison of self-report with data from the regional SEER registry. Eighty five percent of the women who reported that they had had ovarian cancer were not found in the SEER registry. Although some women might have developed their cancers before moving into the Registry area, it is unlikely that this explains the majority of the discrepancies. Family history of ovarian cancer was also reported at a much higher rate than would be expected based on age-specific incidence rates for this area. We concluded that women confused other conditions (e.g., abnormal pap smears or cervical biopsies) with ovarian cancer, and we excluded personal or family history of ovarian cancer from further analyses.

Although 75% of survey respondents had heard “nothing” or “very little” about genetic testing for breast cancer, 65% of respondents were interested in being tested for inherited susceptibility to breast cancer; 46% remained interested in testing even if breast cancer could not be prevented.

In multivariate analyses of factors predicting interest in genetic testing, younger age, family history of breast cancer, and perceived susceptibility to breast cancer were significantly and positively associated with interest in genetic testing; Asian race, less than high school education, better perceived health, and knowledge of genetic testing were significantly and negatively associated with interest in testing.

We reported detailed results of the survey, including tables, in last year’s annual report. During the year covered by this report, data analyses were refined and completed, and work was focused on updating the literature review that had been done for the original proposal. The completed manuscript will be submitted to the journal Genetic Testing in

June 2002. Copies of the completed manuscript will be forwarded to AMRMC at that time.

## 2. Ethnic- Specific Focus Groups

During the last year, 9/1/2000 – 8/31/2001, Drs. Beth Newman and Louisa Collins continued to work on development of their manuscript reporting the results of a qualitative analysis of the ethnic-specific focus groups conducted as part of the second aim of the project. These results were reported in some detail in last year's annual report, so we will only briefly summarize them here. Note that Dr. Newman has continued her work on the project, but has concluded that portion of the project for which she was compensated as a consultant.

We conducted eight ethnic-specific focus groups - two groups each for women who self-identified as African American, Asian, Hispanic, or white - to obtain further information about potential ethnic differences in knowledge about and attitudes toward genetic factors in breast cancer and genetic testing. Each focus group was composed of 4 to 6 women who were selected from those who returned the mailed survey. Each focus group was led by an experienced focus group leader who was also a woman of the same ethnic background as the participants in the group. The groups were videotaped and audiotaped. Meetings lasted about two hours and were held in the evening. Participants were provided sandwiches and drinks and were paid a nominal fee for their time.

A single, standard agenda was followed by all groups. The agenda covered four main areas: a) women's knowledge and opinions about breast cancer in general; b) knowledge and opinions about family history and inherited susceptibility to breast cancer; c) pros and cons of genetic testing for inherited susceptibility to breast cancer and implications of positive or negative test results; d) opinions about how genetic testing should be handled by Kaiser Permanente and how best to inform women about issues such as genetic testing.

For analysis, the videotapes and audiotapes of the focus groups were sent to Dr. Beth Newman, Professor of Public Health, Queensland University of Technology, Kelvin Grove, Queensland, Australia. Dr. Newman, who has been a consultant to the project since its inception, had the tapes transcribed and worked with a graduate student under her supervision, Louisa Collins, to conduct an analysis of the focus groups. Ms. Collins and Dr. Newman conducted a qualitative analysis of the transcribed focus group materials. Verbatim transcripts were reviewed for content and themes, concluding with the coding and analysis of individual statements using a special software developed for qualitative analysis (NUD\*IST).

Four key themes resulted from the analysis: 1) breast cancer knowledge and risk beliefs; 2) knowledge of and attitudes towards family history and breast cancer genes; 3) Attitudes towards genetic testing and the implications, and 4) delivery of information and attitudes towards physicians. In general, the findings from the focus groups paralleled the

results obtained from the survey. Women from all ethnic groups were concerned about developing breast cancer and felt that everyone, regardless of ethnicity, had some degree of risk of developing the disease.

Women from non-white groups expressed more reservations and concerns about reliance on the medical care system for information and advice. White women expressed more confidence in the system, were more comfortable, trustful, and demanding, and reported more positive experiences than women from minority groups. Based on their analysis of the focus group data, Collins, Newman, et al. conclude that "the different education levels, cultures within ethnic groups, and generational differences will prompt the need to develop educational regimes that are multilingual, relatively basic, and sensitive to cultural issues."

During the last year, data analyses were refined and completed. The completed manuscript will be submitted for publication in 2002. Copies of the completed manuscript will be forwarded to AMRMC at that time.

### 3. Follow-up Study of Survey Respondents

The new third aim of the study is to conduct a follow-up study of women who participated in our survey in 1997 to determine how characteristics such as family history of breast cancer, age, and ethnicity, as well as knowledge and attitudes toward genetic testing, are associated with relevant behaviors and medical service utilization during the subsequent 4-5 years of follow-up. We will follow up our survey respondents using two methods. The first method involves record linkage to administrative computerized databases that record all outpatient, inpatient, and pharmacy utilization by Kaiser Permanente Health Plan members. These databases contain information that can be linked to individual survey respondents to indicate the frequency of mammograms, pap tests, and other early detection procedures among survey respondents. We will be able to ascertain whether or not respondents sought genetic counseling, genetic testing, and the educational classes on family history and breast cancer. Pharmacy databases will be used to ascertain the frequency of use of oral contraceptives, Hormone Replacement Therapy, or Tamoxifen among survey respondents. We will analyse the survey data in relation to these outcomes to learn how demographic characteristics, family history of breast cancer, knowledge, and attitudes are related to health behaviors and utilization of preventive services.

During the last year (9/1/2000-8/31/2001), project staff has worked to develop the analysis plans and programming necessary for the follow-up of survey respondents. This has required an ongoing series of meetings to map out and coordinate the data to be obtained from these databases. The task is a large and complex one, since each type of database that will be used (e.g., outpatient visits, pharmacy, or radiology) contains many millions of records and extensive documentation. The databases are maintained by Kaiser Permanente for administrative rather than research purposes. During the last year records for all survey respondents have been successfully linked to several of the

databases that will be used in the study, and downloading of respondent data has been completed for three sources of data to be used in the analyses (i.e., membership records, radiology, and pharmacy).

Looking ahead to the next steps in research on breast and other common cancers, we anticipate that large clinical populations such as Kaiser Permanente's will be sought to participate in research designed to identify the multiple genes and complex gene-environment interactions that are likely involved in the etiology of many common cancers. We believe that it will be important to understand and appreciate possible concerns that people may have about the ethical, legal, and social implications of being involved in this research, and how these concerns vary by ethnicity and other demographic characteristics. Contributing to this conclusion is our conviction that the sequencing of the human genome will usher in a new era of genomic medicine, in which genetic contributions to diseases such as breast cancer will be found (unlike BRCA1/2) to be polygenic, and resulting from complex gene-environment interactions. In this new era, it will no longer be sufficient to inform and educate the relatively small numbers of women whose family histories confer high risk. It will quickly become important to develop strategies for educating the general population about the role of genetics in cancer causation. The potential size of the educational mission for Kaiser Permanente, just as an example, is very large; the northern California Region of Kaiser Permanente, in which this study was undertaken, currently has over 3 million members, including about 1 million women ages 18 and older.

In consideration of the above, and in addition to our follow-up study using electronic databases, we plan to conduct telephone interviews with a stratified random sample of 1,200 of our survey participants in order to update information obtained from the first survey and develop further information on women's knowledge and attitudes toward participation in studies of cancer genomics. We plan to examine possible differences in perspectives, knowledge, and attitudes towards research in this area by interviewing respondents about their responses to pilot consent forms and requests for biospecimens (blood draw or cheek washing).

During the last year, project staff have also worked to complete the new survey that will be administered to 1200 of the original survey respondents in order to measure potential changes in their knowledge and attitudes since the last survey. As part of our planning for the new survey, we have contracted with a survey research group and met to plan their conduct of the survey. The new survey instrument is nearing completion, and we anticipate going into the field for a pilot study in May 2002.

#### **Key Research Accomplishments:**

1. Completion of data analysis and a manuscript based on results of mailed and telephone surveys on 9,877 ethnically diverse women (42% non-Hispanic white, 22% African American, 17% Asian, 18% Hispanic) respondents. This was the first study of family history of breast cancer in large samples of Asian and Hispanic women. It



was also the first study to examine family history and ethnicity in relation to knowledge of and interest in genetic testing in a large, ethnically diverse sample of women with low to moderate risk of inherited susceptibility to breast cancer.

2. Completion of data analysis and a manuscript based on qualitative analysis of ethnic-specific focus groups. These analyses showed differences between ethnic groups in assessment of breast cancer risk factors, although knowledge of breast cancer risk factors, breast cancer genes, and genetic testing was similarly limited and of poor quality among all groups. Analyses indicated that non-whites were more aware of and concerned about negative aspects of genetic testing, including the implications for insurability and employability, the limited value of knowledge from the test, and the difficulty of altering "fate".

### **Reportable Outcomes:**

Schaefer C, Rowell S, Newman B, Bergoffen JA, and Hiatt RA. *The relation of ethnicity and family history to knowledge of and interest in genetic testing in women from a large, multi-ethnic health plan.* Manuscript in preparation, 2002.

Collins C, Newman B, Rowell S, and Schaefer C. *Ethnic differences in knowledge, attitudes, and choices about genetic testing for breast cancer: a qualitative study.* Manuscript in preparation, 2002.

### **Conclusions:**

1. Only 2% of women reported family histories with 2 or more first or second degree relatives with breast cancer. The overwhelming majority of women --about 87% -- reported no family history of breast cancer. Family history varied by ethnicity, with somewhat higher numbers of whites and African Americans reporting family histories that conferred moderate or high risk when compared with the reported family histories of Asian and Hispanic women.
2. Women appeared to confuse ovarian cancer with other cancers or other problems of the reproductive system and made unreliable reports of ovarian cancer in themselves and their relatives.
3. General interest in genetic testing for inherited susceptibility is high, but knowledge of the test and its benefits/costs are low. The more women know about the test, the less interested they were in being tested. Non-whites were more aware of and concerned about negative aspects of genetic testing, including the implications for insurability and employability, the limited value of knowledge from the test, and the difficulty of altering "fate".
4. Knowledge of breast cancer risk factors, breast cancer genes, and genetic testing was similarly limited and of poor quality among all ethnic groups.

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